UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE SELENIOUS ACID LITIGATION	C.A. No. 2:24-cv-07791 (BRM) (CLW) (Consolidated)

DECLARATION OF MICHAEL SWARTZ PH.D.

I, Michael Swartz, have been retained as an expert witness on behalf of Defendants in the above action. I have been asked to prepare this Declaration in support of Defendants' Opposition to Plaintiff's Motion for Preliminary Injunction. If called to testify at a hearing involving such Motion, I expect to give testimony concerning my opinions described in this Declaration.

1) The facts and opinions contained in this Declaration are based on information made available to me in this case on or before the date of this Declaration. I expressly reserve the right to supplement or modify this Declaration if and when I acquire additional relevant information.

2) I have been asked by counsel for Defendants to provide opinions concerning U.S. Pat. Nos. 11,998,565 (the "'565 patent") and 12,150,957 (the "'957 patent," collectively, the "Asserted Patents"). In particular, I have been asked to offer opinions concerning claims 1, 8, and 9 of the '565 patent and claims 1, 6, and 9 of the '957 patent (the "Asserted Claims").

3) I have been asked for my opinion regarding whether a person skilled in the field would find adequate support for the following claim element found in the Asserted Claims: "fluoride in an amount of 0.0001 μg to 2.7 μg per 1 mL of the injectable composition."

This Declaration contains my opinions regarding this issue and the bases for them.

A. Background and Qualifications

4) Briefly, I am a Ph.D. Analytical Chemist with over 40 years of experience, the last 18 of which has been in the Biotech industry. My responsibilities included all Analytical Development testing for both drug product formulations and drug substance across all aspects of Chemistry, Manufacturing and Controls (CMC), from development to commercialization. My test development and validation work supported API and drug product manufacturing and batch release, and formulation development support, including trace elemental analysis as well as impurity analysis and impurity structure elucidation. I have co-authored the CMC sections of IND and NDA applications and amendments (most recently for the FDA-approved drug Cobenfy for schizophrenia); books, chapters, and articles on validation, combinatorial chemistry, and capillary electrochromatography/capillary electrophoresis; over 90 contributed and invited manuscripts; four patents; and over 225 contributed and invited presentations at various technical symposia and conferences around the world. I have served on the Editorial Advisory Board of LC/GC Magazine since 1998. I am a globally recognized leader in analytical chemistry, analytical method development and validation, chromatography, pharmaceutical chemistry, and regulatory compliance. More information on my background and experience is set forth in my *curriculum vitae*, which is attached to this Declaration as Exhibit A.

B. Publications Authored in the Previous 10 Years

5) I have not authored any publications in the previous 10 years.

C. Testimony within Previous Four Years

6) I have not provided testimony as an expert witness in the past 4 years.

D. Fees

7) I am an independent consultant, and I receive compensation of $400/hour, plus reimbursement for any expenses incurred. My compensation does not depend on the opinions I express in this Declaration, my testimony, or the outcome of this case.

E. Preparation and Basis for Opinions

8) Besides conferring with counsel for Defendants, I have performed a number of tasks in preparation for this Declaration. I have been given access to all of the documents produced in this case. I have studied the Asserted Patents, including the Asserted Claims. I have examined the prosecution histories of the Asserted Patents. I have also applied my own knowledge that I have gained over the course of my research career.

9) In presenting the matters set forth in this Declaration at trial, I may use some or all of the documents identified in this section and in attached exhibits, or excerpts and/or enlargements of them. Citations to various sections of documents in this Declaration are not exhaustive, and I may cite additional portions of these documents. I may also use visual aids and demonstrative exhibits to help me explain my opinions, the bases thereof and testimony.

10) Further, I may review additional materials, to supplement my Declaration, and revise the opinions I will present based on any additional reports and testimony of opposing experts, any additional discovery that might occur, further research on the subjects addressed in this Declaration, and testimony and exhibits I otherwise review.

F. The Asserted Patents

11) The ’565 patent issued on June 4, 2024 from U.S. Application No. 18/124,391 (the “’391 Application”) filed on March 21, 2023. The face of the ’565 patent, in Related U.S.

Application Data, cites to two earlier applications, the first is U.S. Application No. 17/365,695 (the "'695 Application") and the second is Provisional Application No. 63/047,708 (the "'708 Provisional"). The '957 patent issued on November 26, 2024 from U.S. Application No. 18/672,876 (the "'876 Application"), filed on May 23, 2024. The '957 patent also includes Related U.S. Application Data, citing to the '391 Application as well as the '695 Application and the '708 Provisional. I have reviewed the '708 Provisional and have been told by counsel to assume that the written descriptions of the '695 Application, the '391 Application, and the '876 Application are all the same.

1. The '565 and '957 Patents

12) The Asserted Claims of the '565 and '957 patents all state: "fluoride in an amount of 0.0001 μg to 2.7 μg per 1 mL of the injectable composition." The Asserted Claims of the '565 patent are as follows:

> 1. An injectable composition comprising water, 6 μg or 60 μg of selenium, no chromium or chromium in an amount not to exceed 1 μg, no aluminum or aluminum in an amount not to exceed 6 μg, no iron or iron in an amount up to 10 μg, and fluoride in an amount of 0.0001 μg to 2.7 μg per 1 mL of the injectable composition.
>
> 8. The injectable composition of claim 1, wherein the injectable composition has a pH of 1.8 to 2.4.
>
> 9. The injectable composition of claim 1, wherein the injectable composition further comprises nitric acid.

(Ex. B ('565 patent).)

The Asserted Claims of the '957 patent are as follows:

> 1. A method of providing an injectable composition to a patient in need thereof, the method comprising administering at least the injectable composition to the patient, the injectable composition comprising water, 6 μg, 40 μg or 60 μg of selenium, no chromium or chromium in an amount not to exceed 1 μg, no aluminum or aluminum in an amount not to exceed 6 μg, no iron or iron in an amount not to exceed 10 μg,

> and fluoride in an amount of 0.0001 μg to 2.7 μg per 1 mL of the injectable composition.
>
> 6. The method of claim 3, wherein the injectable composition comprises nitric acid.
>
> 9. The method of claim 1, wherein the injectable composition has a pH of 1.8 to 2.4.

(Ex. C (’957 patent).)

Counsel has told me that claims 8 and 9 of the ’565 patent and claims 6 and 9 of the ’957 patent incorporate all of the elements of the claims from which they depend, meaning that all of these claims also require the presence of “fluoride in an amount of 0.0001 μg to 2.7 μg per 1 mL of the injectable composition.” Claim 3 of the ’957 patent depends from claim 1.

13) The one and only passage I found in the written descriptions of the Asserted Patents actually disclosing fluoride in connection with the compositions of these patents is as follows:

> In various embodiments, the injectable compositions of this application also include (i) iodine from about 0.0001 to about 0.2 mcg/kg/day, fluoride from about 0.0001 to about 2.7 mcg/kg/day, aluminum from about 0.0001 to about 0.6 mcg/kg/day or a mixture thereof; or (ii) iodine from about 0 to about 0.2 mcg/kg/day, fluoride from about 0 to about 2.7 mcg/kg/day, aluminum from about 0 to about 0.6 mcg/kg/day or a mixture thereof.

(Ex. B (’565 patent) at 17:3-10; Ex. C (’957 patent) at 17: 8-15.) I will call this passage the “Single Passage.” I note that the Single Passage discloses the concentration of fluoride in different units – mcg/kg/day – than the Asserted Claims, which set forth this concentration in μg per 1 ml. In addition to the Single Passage, the Asserted Patents separately disclose fluoride in connection with a “currently available” trace element composition called ADDAMEL™. (Ex. B (’565 patent) and Ex. C (’957 patent) at Table 35.) According to the Asserted Patents, ADDAMEL™ contains “fluoride (95 mcg).”

2. The ’708 Provisional

14) The ’708 Provisional was filed on July 2, 2020. With respect to fluoride, there are three relevant disclosures.

15) First, there is a disclosure, at paragraph [0079], which is nearly identical to the Single Passage:

> In various embodiments, the injectable compositions of this application also include (i) iodine from about 0.0001 to about 0.2 mcg/kg/day, fluoride from about 0.0001 to about 2.7 mcg/kg/day, aluminum from about 0.0001 to about 0.6 mcg/kg/day or a mixture thereof; or (ii) iodine from about 0 to about 0.2 mcg/kg/day, fluoride from about 0 to about 2.7 mcg/kg/day.

(Ex. D (’708 Provisional) at [0079].) Because this disclosure is nearly identical to the Single Passage, I will use the term “Single Passage” to refer to the relevant passage in the ’565 and ’957 patents as well as this passage in the ’708 Provisional.

16) Second, like the Asserted Patents, the ’708 Patent discloses fluoride in connection with ADDAMEL™. (*Id.* at Table 35 (ADDAMEL™ contains “Fluoride (95 mcg)”).)

17) Third, the ’708 Provisional includes dependent claim 4, which states “fluoride from about 0.0001 to about 2.7.” (*Id.* at claim 4.) The units for fluoride are, however, entirely missing in this dependent claim 4.

3. Prosecution Histories

18) My review of the original claims of the ’708 Provisional and the applications that became the Asserted Patents (as well as the patent application to which they claim priority (i.e., the ’695 Application)) reveals that the original claims did not recite the fluoride element as recited by the independent claims issued in the ’565 and ’957 patents. It was not until December 13, 2023 that the Applicants even included claims with fluoride in the claimed concentration.

19) With respect to the '565 patent, the original claims were presented by preliminary amendment. Original independent claim 1 did not recite fluoride and original claim 4 deleted fluoride as follows:

> 1. (Currently Amended) An injectable composition comprising water, and ~~at least one of about 800 µg to about 4,000 µg of zinc, about 40 µg to about 400 µg of copper,~~ about 4 µg to about 90 µg of selenium, no chromium or chromium in an amount not to exceed 1 µg, no aluminum or aluminum in an amount not to exceed 6 µg, and no iron or iron in an amount up to about 10 µg ~~or about 1 µg to about 80 µg of manganese~~ per 1 mL of the injectable composition.

> 4. (Currently Amended) The injectable composition of claim 1, wherein the injectable composition contains ~~further comprising (i) iodine from about 0.0001 to about 0.2 mcg/kg/day, fluoride from about 0.0001 to about 2.7, aluminum from~~ about 0.0001 to about 0.6 mcg of aluminum ~~/kg/day or a mixture thereof~~ per 1 mL~~; or (ii) iodine from about 0 to about 0.2 mcg/kg/day, fluoride from about 0 to about 2.7, aluminum from about 0 to about 0.6 mcg/kg/day or a mixture thereof~~.

(Ex. E ('565 patent file wrapper) at E2 (3/21/23 Original Claims).)

20) In response to a non-final rejection, independent claim 1 was amended to add fluoride with the µg/mL units (underlined below):

> 1. (Currently Amended) An injectable composition comprising water, and about [[4]] 6 µg [[to]] or about [[90]] 60 µg of selenium, no chromium or chromium in an amount not to exceed 1 µg, no aluminum or aluminum in an amount not to exceed 6 µg, [[and]] no iron or iron in an amount up to about 10 µg, and no fluoride or fluoride in an amount up to about 2.7 µg per 1 mL of the injectable composition.

(*Id.* at E136 (12/13/23 Response).) Further, dependent claim 6 was amended to include fluoride in a range of .0001 to 2.7 µg/mL.

> 6. (Currently Amended) The injectable composition of claim 1, wherein the injectable composition contains about 0.0001 µg to about 2.7 µg of fluoride per 1 mL of the injectable composition ~~has a pH of about 1.0 to about 5~~.

(*Id.*) Last, the Applicant argued that the Patent Office's rejection of the term "about" as indefinite was improper because "about" should mean +/- 10%:

> For example, and not to be limiting, it is known in the pharmaceutical arts that the amount of the drug on the label is not an exact amount but will be within 90% to 110% of the amount indicated on the label as described in Tables 2 and 30 of the current specification.

(*Id.* at E142 (Remarks).)

21) In a Final Rejection, the Patent Office stated that the term "about" when used with selenium was indefinite because it has no universal metes and bounds and also maintained prior art rejections. (*Id.* at E164 (2/1/24 Final Rejection).) The Final Rejection did not address fluoride in connection with the prior art. In response to the Final Rejection, the '565 patentee interviewed the Patent Examiner. The parties agreed that independent claim would be allowable if rewritten to include the text of dependent claim 6. (*Id.* at E174 (02/28/24 Interview Summary).) The next filing by the '565 patentee included this amendment:

> 1. (Currently Amended) An injectable composition comprising water, ~~and about~~ 6 µg or ~~about~~ 60 µg of selenium, no chromium or chromium in an amount not to exceed 1 µg, no aluminum or aluminum in an amount not to exceed 6 µg, no iron or iron in an amount up to ~~about~~ 10 µg, and ~~no fluoride or~~ fluoride in an amount of 0.0001 µg [[up]] to ~~about~~ 2.7 µg per 1 mL of the injectable composition.

(*Id.* at E176 (03/1/24 Amendment).)

22) The Patent Office allowed the application and provided the following Reasons for Allowance:

> The following is an examiner's statement of reasons for allowance: the prior art lacks a teaching or suggestion of a composition comprising selenium and fluoride in an amount of 0.0001-2.7µg. The prior art teaches composition comprising selenium. The prior art also teaches composition comprising fluoride. However, the prior art does not teach or suggest a composition having fluoride in an amount of 0.0001-2.7µg. Therefore, claims 1-6, 8, 9, 11, 13-19. 63, 65-70, and 74-79 are allowed.

(*Id.* at E194 (3/22/24 Notice of Allowance).)

23) The application that became the '957 patent was filed on May 23, 2024. Original claim 56 (which became independent claim 1) was as follows:

> 56. (Currently Amended) A method of ~~maintaining plasma~~ providing an injectable composition to ~~trace elements in~~ a patient in need thereof, the method comprising administering at least [[an]] the injectable composition to the patient, the injectable composition comprising water, ~~and at least one of about 800 µg to about 4,000 µg of zinc, about 40 µg to about 400 µg of copper, about 4~~ 6 µg, 40 µg or ~~to about 90~~ 60 µg of selenium, no chromium or chromium in an amount not to exceed 1 µg, no aluminum or aluminum in an amount not to exceed 6 µg, no iron or iron in an amount not to exceed 10 µg, and fluoride in an amount of 0.0001 µg to 2.7 µg ~~or about 1 µg to about 80 µg of manganese~~ per 1 mL of the injectable composition.

(Ex. F ('957 patent file wrapper) at F95 (5/23/24 Original Claims).)

24) On September 5, 2024, a Notice of Allowance was mailed. (*Id.* at F103 (9/5/24 Notice of Allowance).) The Reasons for Allowance in the Notice of Allowance were the same as the Reasons for Allowance given in the application that became the '565 patent. (*Id.* at F108-F109.) A supplemental Notice of Allowance with the same Reasons for Allowance was mailed on October 9, 2024. (*Id.* at F114 (10/9/24 Notice of Allowance).)

G. Written Description Analysis

25) It is my opinion that all Asserted Claims are invalid for lack of written description because a person skilled in the field would not understand the inventors, at the time of filing the Asserted Patents (or the patents to which they claim priority), to have possessed compositions with the claimed range of fluoride concentration. The written descriptions of neither the Asserted Patents nor the '708 Provisional demonstrates possession of the fluoride element found in all the Asserted Claims.

1. Legal Instructions

26) I have been told by counsel that a patent claim is invalid if the patent does not contain an adequate written description of the claimed invention from the perspective of one ordinary skill in the art. I am at least one of ordinary skill in the art and have provided my opinions herein from the perspective of such a person of ordinary skill.

27) I understand the test for written description is whether the specification would have objectively demonstrated to a person skilled in the field that the patent applicant actually invented, or "possessed," the claimed elements when the patent application was filed. I have been told that inventors can show possession by an express disclosure of an embodiment encompassing all the elements of the claims or by other disclosures that lead the skilled person to conclude the elements are present both individually and in combination. I recognize the written description requirement does not require disclosure of examples or the manufacturing of an actual prototype of the claimed invention. However, the written description must show possession of the invention by the inventors, and evidence of reduction to practice outside of the specification is not sufficient by itself to satisfy the written description requirement.

28) Finally, I have been told to assume that all claims depending from the independent claims in the Asserted Patents recite all the same elements as the independent claims from which they depend.

2. Analysis

29) A person skilled in the field would not understand the inventors to have possessed the claimed compositions. There is no express disclosure in the Asserted Patents and the '708 Provisional of "fluoride in an amount of 0.0001 μg to 2.7 μg per 1 mL of the injectable composition." And there is no disclosure that suggests to a person skilled in the field that the fluoride element was part of the invention. There are multiple reasons why I believe the Single Passage does not demonstrate possession of this fluoride element.

30) First, use of the Single Passage's lead-in phrase "[i]n various embodiments" means that not every embodiment of the injectable compositions disclosed in the written description includes the listed fluoride element. To that end, I have not found a single specific composition, embodiment, or example in the written descriptions of the Asserted Patents and '708 Provisional containing the components listed in the independent claims under review. It is unclear, in my opinion, which embodiments the Asserted Patents and '708 Provisional contemplate should and should not contain these claimed elements. I have also found no disclosure elsewhere in the patent clarifying this point.

31) This is important because the independent claims of the Asserted Patents all set forth specific embodiments. For example, the claim 1 composition of the '565 patent contains water, selenium, no chromium or chromium in an amount not to exceed 1 μg, no aluminum or aluminum in an amount not to exceed 6 μg, and no iron or iron in an amount up to 10 μg. Not only does the '565 patent fail to expressly disclose the specific combination of these elements in

a single embodiment, it discloses at least millions of potential permutations of different embodiments that may or may not include them.

32) The Summary of Invention, for example, refers to millions of different embodiments. One embodiment lists multiple combinations of components that do not together appear in any of the claims of the '565 and '957 patents, including zinc, copper, and manganese:

> In one embodiment, there is an injectable composition comprising water, and at least one trace element consisting of about 800 μg to about 4,000 μg of zinc, about 40 μg to about 400 μg of copper, about 4 μg to about 90 μg of selenium, or about 1 μg to about 80 μg of manganese per 1 mL of the injectable composition.

(Ex. B ('565 patent) at 3:1-6; Ex. C ('957 patent) at 3:1-6.) Because this passage uses the phrase "at least one trace element," it discloses 64 different combinations of trace elements and potentially millions of different embodiments based on the wide ranges of different combinations of concentrations of such trace elements. Further, the Asserted Patents disclose that the trace elements themselves may come in different forms:

> In many aspects, the zinc in the injectable composition is elemental zinc, the copper is elemental copper, the selenium is elemental selenium, the manganese is elemental manganese and the water is sterile water for injection. In other instances, the elemental zinc is obtained from zinc sulfate or zinc sulfate heptahydrate, the elemental copper is generated from cupric sulfate or cupric sulfate pentahydrate, the elemental manganese is from manganese sulfate or manganese sulfate monohydrate and the elemental selenium is obtained from selenious acid.

(Ex. B ('565 patent) at 10:43-52; Ex. C ('957 patent) at 10:40-49.) Starting with nine possible ingredients for compositions containing between 1 to 9 ingredients increases the number of possible embodiments from 64 to 986,409.

33) The Summary of Invention also discloses that "in many embodiments," the injectable compositions can be combined with "an amino acid, dextrose, a lipid, an electrolyte, or a mixture thereof." When combined with the trace elements, the total number of embodiments increases further still.

34) The Asserted Patents go on to include countless additional embodiments. The Asserted Patents disclose the potential inclusion of numerous other compounds, increasing the number of embodiments exponentially:

> In other embodiments, the injectable composition of this application also includes (i) iron from about 0.0001 to about 10 g/mL, silicon from about 0.0001 to about 100 µg/mL, magnesium from about 0.0001 to about 50 µg/mL, calcium from about 0.0001 to about 50 µg/mL, boron from about 0.0001 to about 50 g/mL or a mixture thereof; or (ii) iron from about 0 to about 10 µg/mL, silicon from about 0 to about 100 µg/mL, magnesium from about 0 to about 50 g/mL, calcium from about 0 to about 50 µg/mL, boron from about 0 to about 50 g/mL or a mixture thereof.
>
> In some embodiments, the permitted daily limits (PDL) of the injectable trace elements of the current application are not to exceed about 0.4 µg/day of cadmium, about 0.5 µg/day of lead, about 1.5 µg/day of arsenic, about 0.4 µg/day of mercury, about 1 µg/day of cobalt, about 2 µg/day of vanadium, about 4 µg/day of nickel, about 1.6 µg/day of thallium, about 20 µg/day of gold, about 2 µg/day of palladium, about 2 µg/day of iridium, about 2 µg/day of osmium, about 2 µg/day of rhodium, about 2 µg/day of ruthenium, about 2 µg/day of silver, about 2 µg/day of platinum, about 50 µg/day of lithium, about 18 µg/day of antimony, about 140 µg/day of barium, about 300 µg/day of molybdenum, about 120 µg/day of tin, about 1 µg/day of chromium, about 6 µg/day of aluminum, about 50 µg/day of boron, about 50 µg/day of calcium, about 10 µg/day of iron, about 94,000 µg/day of potassium, about 50 µg/day of magnesium, about 24,000 µg/day of sodium, about 1 µg/day of tungsten, and/or about 100 µg/day of silicon.

(Ex. B (’565 patent) at 17:10-20, 15:12-19; Ex. C (’957 patent) at 17:15-25, 15:3-18, 16:1-2.)

35) Next, the Asserted Patents state that the injectable compositions may contain impurities, adding still more embodiments to the millions already disclosed:

> While these injectable compositions contain little or no impurities, in some aspects, these compositions can include a chromium impurity.
>
> In various embodiments, other elemental impurities, for example, lead, arsenic, cadmium, mercury iron, chromium (potential manufacturing process contaminants) and boron, calcium, magnesium, and silicon (potential leachable elemental impurities from the drug product Type I glass vials and West elastomeric formulation 4432/50 grey stopper used as immediate packaging) have been considered.

(Ex. B (’565 patent) at 13:54-56, 14:57-63; Ex. C (’957 patent) at 13:44-46, 13:61-67.)

Then there is the Single Passage disclosing fluoride, iodine and aluminum, which I identified at the outset. (Ex. B (’565 patent) at 17:3-9; Ex. C (’957 patent) at 17:8-14.) There is also, incorporation of a preservative in some embodiments: “The preservative can, be in some cases, benzyl alcohol.” (Ex. B (‘565 patent) at 18:4-9; Ex. B (‘957 patent) at 18:17-19.)

36) The Asserted Patents provide no direction concerning which of the “various embodiments” referred to in the Single Passage are supposed to include fluoride. Thus, in my opinion, those of ordinary skill in the field either are left guessing which of the millions of embodiments disclosed by the Asserted Patents include fluoride or would have to use hindsight when selecting from the multitude of ingredients and concentrations in the specification to arrive at the claimed composition. As I mentioned, the written descriptions of the Asserted Patents not once expressly mention a single embodiment containing each of the ingredients set forth in the independent claims of the Asserted Patents with fluoride. They certainly do not mention the specifically claimed compositions as embodiments contemplated by the inventors when the applications leading to the Asserted Patents were filed.

37) Second, comparing the Single Passage to the independent claims, it is clear the units used for fluoride in each differ. The Single Passage uses “mcg/kg/day.” In contrast, the claims use “µg per 1 mL of the injectable composition.” The former relates to the quantity of fluoride to administer based on the weight of the patient while the latter relates to the quantity of fluoride in a composition based on its volume. The Asserted Patents provide no disclosure that directs one to the specific ranges claimed.

38) The Single Passage provides no basis for the patentee to use the numerical range .0001 to 2.7 µg per 1 mL for fluoride in the first place. This range with these endpoints does not

appear anywhere in the Asserted Patents besides the claims. A person skilled in the field would immediately recognize mcg/kg/day and µg/mL are entirely different units of measure and calculations are required before the claims can be amended with numerical values identified for the former (mg/kg/day) with the different units for the latter (µg/mL).

39) Regarding such calculations, I have found nothing in the written descriptions of the Asserted Patents that expressly explains how to convert one set of units to the other. The calculation, which I have experience with, is as follows:

Concentration (mcg/ml) = Dosage (mcg/kg/day)*Patient Weight (kg)/Infusion Volume (ml/day)

I have thus reviewed the Asserted Patents for other disclosures relevant to such a calculation. There is a disclosure appearing in Table 3 that provides the maximum daily dose (MDD) for the trace element composition along with body weights for patients.

TABLE 3

Dosing Requirements in mL/kg Body Weight for Trace Element Compositions

Patient Group	Body Weight	MDD (mL)
Adult	≥50 kg	1 mL
Pediatric	40 kg to 49 kg	0.8 mL
Pediatric	30 kg to 39 kg	0.6 mL
Pediatric	20 kg to 29 kg	0.4 mL
Pediatric	10 kg to 19 kg	0.2 mL

(Ex. B ('565 patent) at Table 15:1-11; Ex. C ('957 patent) at 14:48-60.) The MDD is the maximum dose in mL that patients of these different body weights should receive per day. In other words, the MDD represents the highest possible per day dosing for purposes of converting mcg/kg/day to µg/mL.

40) Because the written descriptions of the Asserted Patents do not state the purpose of Table 3, specify the concentration of ingredients that should be used to make the "Trace Element Compositions" that are the subject of Table 3, or make any express connection between the Single Passage and Table 3, it is unclear that a person of ordinary should use Table 3 to

convert mg/kg/day to µg/mL. Further, the written descriptions never state or imply that Table 3 should apply to all disclosed compositions. Assuming Table 3 applies to the Single Passage, a conversion can be made. As one example, if an MDD of 1 mL per day is used as the basis for calculations in an adult patient weighing 75 kg, the fluoride concentration would be 75 kg x (0.0001 mcg to 2.7 mcg) mcg/kg/day ÷ 1 mL = 0.0075 – 202.5 mcg/day. Since the (MDD) for an adult patient of 75kg is 1 mL this equals 0.0075 – 202.5 mcg/mL or 0.0075 to 202.5 µg/mL. Assuming other body weights for adult and pediatric patients, I converted the mcg/kg/day endpoint values from the Single Passage (e.g., 0.0001 mcg/kg/day and 2.7 mcg/kg/day) to the following values for fluoride in "µg per mL":

Pediatric weight	MDD	F content (µg /mL)
10 kg	0.2 mL	0.005 - 135
20 kg	0.4 mL	0.005 - 135
30 kg	0.6 mL	0.005 - 135
40 kg	0.8 mL	0.005 - 135
49 kg	0.8 ml	0.006 - 165
Adult weight	MDD	F content (µg /mL)
50 kg	1 mL	0.005 - 135
60 kg	1 mL	0.006 - 162
70 kg	1 mL	0.007 - 189
80 kg	1 mL	0.008 - 216
90 kg	1 mL	0.009 - 243
100 kg	1 mL	0.01 - 270
110 kg	1 mL	.011 - 297
120 kg	1 mL	.012 - 324

Especially for adults, as body weight increases and the volume given is 1 mL per day, the endpoint values in the range are even larger. For example, 67.5 kg (about 150 pounds) would result in a fluoride concentration of up to 185 µg/mL, 95 kg (about 210 pounds) would result in a fluoride concentration up to 257 µg/mL, 100 kg (about 225 pounds) would result in a fluoride concentration up to 270 µg/mL, and a 115 kg (250 pounds) would result in a fluoride concentration of up to 306 µg/mL.

41) Based on the foregoing and assuming a converted range can be created based on the disclosures, the following chart is a summary of the situation using a hypothetical 210-pound person:

Disclosed fluoride endpoints (mcg/kg/day)	**Disclosed fluoride endpoints after conversion using person weighing 210 pounds (µg/mL)**	**Claimed fluoride endpoints (µg/mL)**
0.0001 mcg/kg/day to 2.7 mcg/kg/day	0.0095 µg/mL to 257 µg/mL	0.0001 µg/mL to 2.7 µg/mL
0 mcg/kg/day to 2.7 mcg/kg/day	0 µg/mL to 257 µg/mL	0.0001 µg/mL to 2.7 µg/mL

42) The above calculations demonstrate that the range for fluoride in mcg/kg/day in the Single Passage are dramatically different from the range for fluoride in µg/ml in the independent claims of the Asserted Patents. Further, none of the values that I converted from mcg/kg/day to mcg/day above are even close to the bottom end of the claimed range for fluoride (i.e., 0.0001 µg per one mL) or the top end (i.e., 2.7 µg per one mL). After conversion, the lowest value for the bottom end of fluoride concentrations in the Single Passage is 0.005 µg/mL, which is fifty times greater than the 0.0001 µg/mL concentration stated for fluoride in the claims.

43) Similarly, none of the values calculated for the top end of the range in the Single Passage are even close to the claimed top end of the claimed range for fluoride (i.e., 2.7 µg per one mL for fluoride). For instance, fluoride at a concentration of 135 µg and 257 µg differs significantly from 2.7 µg.

44) Thus, in my opinion, a person skilled in the field would not understand the inventors to have possessed the claimed fluoride concentration range. Any assertion by Plaintiff that the term “about” in the specifications somehow bridges these large gaps is incorrect. With respect to “about,” I note that the Asserted Patents state as follows:

> For the purposes of this specification and appended claims, unless otherwise indicated, all numbers expressing quantities of ingredients, percentages or proportions of materials, reaction conditions, and other numerical values used in the specification and claims, are to be understood as being modified in all instances by the term "about." Accordingly, unless indicated to the contrary, the numerical parameters set forth in the following specification and attached claims are approximations that may vary depending upon the desired properties sought to be obtained by the present disclosure. At the very least, and not as an attempt to limit the application of the doctrine of equivalents[1] to the scope of the claims, each numerical parameter should at least be construed in light of the number of reported significant digits and by applying ordinary rounding techniques.

(Ex. B ('565 patent) at 5:32-46.) I was asked to interpret "about" as one skilled in the field would interpret it. In this regard, I note that the '565 patentee itself asserted that "about" only covers a +/- 10% difference. (Ex. E ('565 patent file wrapper) at E142 (12/13/23 Response).) Thus, the 50x difference between the concentrations calculated after converting mcg/kg/day into µg/mL for the Single Passage and the concentrations in the claims is far too great for the patentee to take advantage of the term "about" in column 17.

45) The Asserted Patents also state that numerical values contain errors resulting from standard deviations in their testing measurements and that all ranges are to be understood to encompass subranges subsumed therein:

> Any numerical value, however, inherently contains certain errors necessarily resulting from the standard deviation found in their respective testing measurements.
>
> Moreover, all ranges disclosed herein are to be understood to encompass any and all subranges subsumed therein. For example, a range of "1 to 10" includes any and all subranges between (and including) the minimum value of 1 and the maximum value of 10, that is, any and all subranges having a minimum value of equal to or greater than 1 and a maximum value of equal to or less than 10, e.g., 5.5 to 10.

[1] I am told that the doctrine of equivalents relates to infringement as opposed to the issues I am analyzing and have not offered opinions concerning the doctrine of equivalents.

(Ex. B ('565 patent) at 5:50-60; Ex. C ('957 patent) at 5:49-59.) Neither of these points bridges the gap between the Single Passage and the claims. First, if anything, the fact that numerical values "inherently contain certain errors" makes the values found in the written description and claims unreliable. Second, even assuming such values are reliable, a standard deviation used in measurement techniques for fluoride would not in my opinion ever encompass a 50x difference. Second, even assuming the ranges encompass subranges, the calculations for the bottom end of the fluoride range as 0.005 µg/mL is miles away from 0.0001 µg/mL. Further, to the extent Plaintiff relies upon the disclosure in the Single Passage stating that fluoride can be present "from about 0 to about 2.7mcg/kg/day," the top of the range of – 2.7 mcg/kg/day converted to 324 µg/ml – renders the total range so exceedingly broad that one of ordinary skill would not envision or arbitrarily pick 0.0001 µg/ml to 2.7 µg/ml, as the Asserted Patents do here.

46) In addition to all of the foregoing problems, the number of different patient weights and MDDs used in calculations necessary to convert the units in the Single Passage to the units set forth in the claims creates millions of more embodiments. The combinations of body weight and MDD are endless, with countless permutations. The disclosed body weights are 10 kg, 20 kg, 30 kg, 40 kg, 49 kg, 50 kg, 60 kg, 70 kg, 80 kg and beyond, and patients could receive virtually any reasonable amount of the injectable composition less than the MDD per day (e.g., an adult could receive 0.4 mL, 0.5 mL, 0.6 mL, 0.7 mL, 0.8 mL, etc.).

47) In sum, the only way a person skilled in the field would know that the injectable compositions from the Asserted Patents should contain or possessed fluoride in the range of 0.0001 to 2.7 mcg/mL is by looking at the claims themselves.

48) In addition, and more generally, the written descriptions in the Asserted Patents and '708 Provisional fail to disclose the process for ensuring the claimed ranges of fluoride.

They fail to state that fluoride should be minimized in the injectable compositions or what standards, methods, or tests to employ to determine whether, and to what extent, fluoride exists in the injectable compositions. Nor do they explain a method or how to validate a method for determining concentrations of fluoride down to detectable limits of 0.0001 µg. For instance, while Example 7 provides a process for preparing a trace element composition, it does not mention fluoride at all. Further, I am not aware of an industry-accepted validated method for measuring fluoride in the amounts set forth in the claims.

49) In addition, the written descriptions of the Asserted Patents and '708 Provisional are extremely confusing as to whether fluoride is an intentionally added trace element component of the injectable compositions as opposed to a contaminant or impurity. (*See* Ex. B ('565 patent) at 16-17; 12:32-33 ("Elemental Impurities of Trace Elements Injectable Composition"); Ex. B ('957 patent) at 16-17; 12:26-27.)

50) These written descriptions never expressly identify fluoride as an impurity. In contrast, they describe several other "elemental impurities" and their upper limits in Tables 2 and 4. In fact Table 4 identifies elemental impurity limits for a total of 31 separate elements. Fluoride is nowhere to be found. Similarly, Table 30 also discloses elemental impurities with upper limits, including aluminum, arsenic, mercury, cadmium, chromium, iron, silicon, magnesium, calcium, and boron. Fluoride is not mentioned and there is no indication of a permissible concentration or range for fluoride or any testing methodology for determining whether fluoride is present. (Ex. B ('565 patent) at Table 30; Ex. C ('957 patent) at Table 30). I have found nothing in the written descriptions of the Asserted Patents and the '708 Provisional that would allow me to verify the fluoride concentrations of the Asserted Claims or that such fluoride concentration needs to be limited to between 0.0001 µg /mL and 2.7 µg /mL.

51) Because none of this information is contained in the written description of the Asserted Patents, a December 2023 declaration submitted by Dr. Richard Lawrence to the U.S. Patent Office during prosecution of the '565 patent states "during manufacturing… we needed to make sure no chromium, iron, fluoride, iodine, and/or silicon or very low amounts of these were not above our established permitted daily limits (PDL) and our new control thresholds for impurities." (Ex. E ('565 patent file wrapper) at E120 (Declaration of Richard Lawrence at 2 (Dec. 13, 2023)).) The same declaration cites many potential sources of, e.g., fluoride, including the active selenium ingredient, excipients, stopper, vial, mixing vessels, filter, water, and air. In addition to the drug substance, selenious acid, the drug product manufacturing process, equipment and container/closure components can be a source of impurities. (*Id.*)

52) On the other hand, the top end of the range of fluoride after conversion indicates to one of ordinary skill that fluoride should be intentionally added to the composition. Further, discussion in the specifications of the "currently available" ADDAMEL™ composition with its intentionally added 95 mcg/mL concentration of fluoride, supports intentional addition. Indeed, this concentration of fluoride is higher than the concentration of claimed selenium, which is the main ingredient intentionally added to the claimed injectable composition. Further, fluoride is added to everything from water to toothpaste and I am unaware of any industry limits of 0.0001 µg/mL to 2.7 µg/mL. This confusion makes it especially difficult for one of ordinary skill to determine the intended purpose of the fluoride in the Single Passage or to somehow arrive at a range of 0.0001 to 2.7 µg/ml of fluoride as the patentee did here during examination to get its claims allowed. Indeed, nothing in the disclosure would lead a person of skill to even measure the amount of fluoride in the injectable compositions of the Asserted Patents. Given the Single Passage encompasses fluoride values greater than 200 µg/mL, and the totality of the written

description's lack of any reference to fluoride as a contaminant, there is nothing suggesting that fluoride needs to be minimized in any way.

53) Further, the written descriptions of the Asserted Patents fail to explain anything about possible sources of fluoride. In contrast, if the intent is to intentionally add fluoride, there is no disclosure about how, when, or where this component should be added. In addition, while the written descriptions describe PDLs for chromium, iron, and silicon, they do not disclose any information about fluoride besides the Single Passage indicating the injectable compositions of this application also include mcg/kg/day amounts of fluoride that differ substantially from the claimed ranges.

54) Other than the Single Passage and passing reference to ADDAMEL™, the written descriptions of the Asserted Patents do not provide a permissible amount or range for fluoride for inclusion in the injectable compositions. Nor do the written descriptions explain the difference in units set forth in the Single Passage and the claims or why one correlates with the other. There is certainly no disclosure of a testing methodology for fluoride or evidence that the inventors possessed a test for determining fluoride concentrations in the injectable compositions.

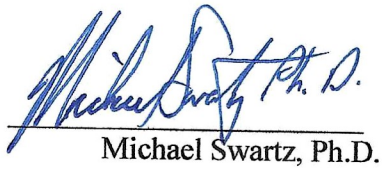
55) Finally, it is my opinion that none of the asserted dependent claims recites anything that would lead a person skilled in the field to understand the inventors possessed the claimed fluoride concentration range and save the independent claims. They do not for example set forth concentrations of fluoride in mg/kg/day or anything else consistent with these values.

Conclusion

56) The foregoing opinions and bases for them are current to the date of my signature below, and are based on the information disclosed in this case up to this date. I reserve the right to supplement my opinions in light of further information disclosed in the case. I also reserve the right to supplement my Declaration to rebut any opinions expressed by any experts retained by the plaintiff.

I declare under penalty of perjury of the laws of the United States that the foregoing is true and correct.

Executed at Cotuit, Massachusetts
February 7, 2025



Michael Swartz, Ph.D.